REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-209 are pending in the application. Claims 1-7, 9-13 and 15-209 are withdrawn. The Examiner rejected claims 8 and 14. Claim 8 has now been canceled, rendering moot the Examiner's rejection thereof. Claims 1, 14-18, 20, 33-37, 39, 52-56, 58, 71-75, 77, 90-94, 96, 109-113, 115, 128-134, 147-151, 153, 166-170, 172, 183-187, 189 and 202-206, have been amended. Amendments to claims 1, 14-18, 20, 33-37, 39, 52-56, 58, 71-75, 77, 90-94, 96, 109-113, 115, 128-134, 136, 147-151, 153, 166-170, 172, 183-187, 189 and 202-206 are supported throughout the specification as originally filed, and as such do not constitute addition of new subject matter.

Abstract and Specification Objections

In the Office Action, the Examiner objected to the inclusion of embedded hyperlinks, for example, in the abstract, claims and elsewhere throughout the disclosure. The cited hyperlinks (for example, **http://www.ch.embnet.org/index.html**) have now replaced with term inactivating the hyperlinks such as: (**http://wwwdotch.embnetdotorg/index.html**), and thus do not now include an embedded hyperlink. Amended Specification, Abstract and Claims are found hereinabove. Accordingly, Applicant requests withdrawal of the objection.

35 U.S.C. § 101 Rejections

The Examiner has stated that claims 8 and 14 are rejected under 35 U.S.C. § 101 for not being supported by an asserted or well established utility. Claim 8 has now been cancelled, rendering moot the Examiner's rejection thereof. Claim 14 has now been amended. The Examiner's rejection is respectfully traversed.

The specific structure of the claimed variant of Met (termed hereinafter "Met-934" as it is 934 amino acids long) and its asserted function is described on the last paragraph of page 80, and also on page 81 (paragraphs 463-468 of the application as published). It should be noted, as stated in paragraph 464, that this section relates to a single Met variant according to SEQ ID NOs 1 and 3. In particular, paragraph 466 describes the structure and expected biological actions and activity of the Met splice

variant (Met-934; see also Figure 4):

> Met splice variant of the present invention can serve as a antagonist (i.e., inhibitor) of Met-HGF interaction. It contains the extracellular region of Met, the HGF binding site, and therefore it is likely to bind HGF. Met extracellular region has been shown previously to bind HGF with a high affinity (comparable to the membrane bound receptor). Met splice variant can inhibit Met-HGF signaling by competing with the membrane-bound receptor for the ligand-HGF, thus preventing HGF binding to the cell surface receptor and as a consequence blocking Met activation and its signaling pathway.

Paragraph 467 describes methods of use of the Met splice variant according to the present invention for treatment of various cancers:

> Because of the overwhelming evidence favoring the role of aberrant HGF-Met signaling in the pathogenesis of various human cancers, endogenous and exogenous inhibitors of this signaling pathway such as Met splice variant may be used as valuable therapeutic tools in the treatment of cancers such as, hereditary and sporadic papillary renal carcinoma, breast cancer, ovarian cancer, childhood hepatocellular carcinoma, metastatic head and neck squamous cell carcinomas, lung cancer (e.g., non-small cell lung cancer, small cell lung cancer), prostate cancer, pancreatic cancer, gastric cancer and other diseases such as diabetic retinopathy.

Thus, the specific structure, functionality and utility of Met-934 are clearly described. Furthermore, the clearly asserted and described utility is supported by experimental data, as described in greater detail below and also in the attached affidavit.

Thus, Applicant respectfully requests withdrawal of the 35 U.S.C. §101 rejection.

35 U.S.C. § 112 1st Paragraph Rejections

The Examiner has rejected claims 8 and 14 under 35 U.S.C. § 112 1st Paragraph as failing to comply with the written description requirement, for containing subject matter which was not described in the specification in such a way as to reasonable convey that the inventors had possession of the claimed invention. Claim 8 has been cancelled, rendering moot the Examiner's rejection thereof. Claim

14 hasnow been amended. The Examiner's rejection is respectfully traversed.

Claims 8 and 14 are rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement. Applicant respectfully traverses. The nucleotide sequence of Met-934 is clearly given as being SEQ ID NO:3 (see above and also Figure 1a), while the amino acid sequence is clearly given as being SEQ ID NO:1 (see above and also Figure 1b). Neither claim 8 nor claim 14 currently recite fragments or portions. The term "fragments" in paragraph 184 is not intended to refer to the full length sequence which actually encodes the claimed amino acid sequence, which represents the full length of Met-934 (SEQ ID NO:1). Instead, the term relates to the separately described amino acid sequence(s) for active portions of Met-934. Thus, the claims currently clearly recite the complete sequence of Met-934, such that the nucleotide sequence and amino acid sequence are clearly supported in the text.

Thus, Applicant respectfully requests withdrawal of the 35 U.S.C. 112 1st paragraph rejections.

35 U.S.C. § 112 2nd Paragraph Rejections

The Examiner has rejected claims 8 and 14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Claim 8 has now been cancelled, rendering moot the Examiner's rejection thereof. Claim 14 has now been amended. The Examiner's rejections are respectfully traversed.

As agreed upon in the meeting of October 30, 2006, Claim 14 has now been amended to read "an isolated polypeptide consisting essentially of an amino acid sequence according to SEQ ID NO: 1". The Examiner agreed in the interview with the representative of Applicant that such an amendment would suffice to overcome these rejections.

35 U.S.C. § 102 Rejections- US Patent Application No. 2003/0118585 to Muller et al

The Examiner has rejected claims 8 and 14 under 35 U.S.C. § 102(e), as allegedly being anticipated by Muller et al (Patent Application No. 2003/0118585 to Muller et al., hereinafter "Muller"). Claim 8 has now been cancelled, rendering moot

the Examiners rejection thereof. Claim 14 has now been amended. Applicant disagrees.

The Examiner states that Muller teaches an isolated polypeptide sequence wherein SEQ ID NO. 12 is 97.6% identical to instant SEQ ID NO. 1. In fact, SEQ ID NO:12 teaches the complete sequence of c-Met (the known or wild type protein) and thus has an overall homology to SEQ ID NO:1 that is much lower than 97.6%, specifically, 67% (SEQ ID NO: 1 corresponds to the amino acids 1-910 of full length human c-Met, which is 1339 nucleotides in length). However, Applicant wishes to draw the Examiner's attention to a reference, included in the IDS filed with this response: Mark et al., 1992, J Bio. Chem., 267:26166-26171, hereinafter referred to as "Mark 1992". This reference teaches that the extracellular domain of c-Met ranges from amino acid residue 1 to 929, and that this extracellular domain may be expressed as a separate, soluble protein. The results of a BLAST comparison between SEQ ID NO:1 and the extracellular domain of c-Met clearly demonstrate that there are significant homology differences between SEQ ID NO:1 of the present invention (Met-934) and the extracellular domain of c-Met as taught in the reference. In particular, only the first 910 amino acids are shared, such that there is a unique portion of the end of applicant's Met-934 variant that is 24 amino acids in length.

With regard to the rejections of claims 8 and 14 over Park et al (PNAS USA 1987 84:6379-83), Applicant notes that claim 8 has been canceled without prejudice, rendering moot the rejection thereof. Claim 14 has now been amended to recite "an isolated polypeptide consisting essentially of an amino acid sequence according to SEQ ID NO: 1". Therefore, according to understandings reached with the Examiner during the interview, this amendment places the scope of the claim outside of the teachings of Park et al, which relate only to a polypeptide wherein residues 1-755 are 97.6% identical to SEQ ID NO:1.

In view of the foregoing amendments and remarks, and in view of the affidavit enclosed herewith, the pending claims are deemed to be allowable. Their favorable reconsideration and prompt notice of allowance is respectfully solicited.

Respectfully submitted,

Martin D. Moynihan
Registration No. 40,338

Date: December 26, 2006

Enclosed:
Petition For Extension (1 Month);
Declaration of Dr. Michal Ayalon-Soffer;
Figures for Declaration; and
Curriculum Vitae of Dr. Michal Ayalon-Soffer.